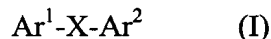


WHAT IS CLAIMED IS:

1. A method of treating a CCR4-mediated condition or disease in a subject, said method comprising administering to a subject in need of such treatment an effective amount of a compound having the formula:



wherein

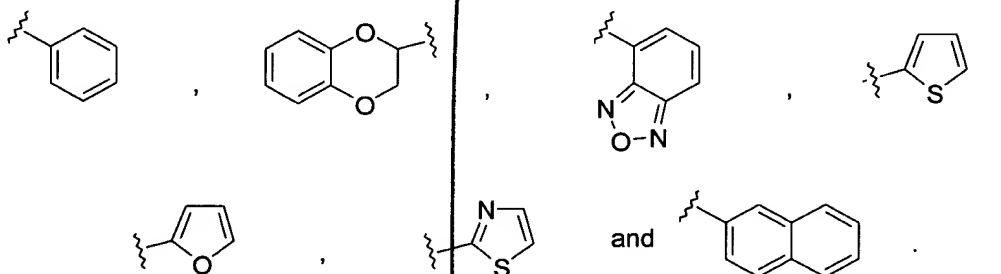
Ar^1 and Ar^2 are each members independently selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted fused aryl-heterocyclic ring systems and substituted or unsubstituted heteroaryl; and

X is a linking group selected from the group consisting of -N(R)- , -C(O)S- , $\text{-CH=CHSO}_2\text{-}$ and $\text{-SO}_2\text{N(R)-}$ wherein R is a member selected from the group consisting of H and substituted or unsubstituted $(\text{C}_1\text{-C}_8)\text{alkyl}$.

2. A method in accordance with claim 1, wherein X is -NH- .

3. A method in accordance with claim 1, wherein X is $\text{-SO}_2\text{NH-}$.

4. A method in accordance with claim 1, wherein Ar^1 and Ar^2 are each substituted or unsubstituted members independently selected from the group consisting of:



5. A method in accordance with claim 2, wherein Ar^1 is substituted heteroaryl and Ar^2 is substituted or unsubstituted aryl.

6. A method in accordance with claim 5, wherein said Ar^1 is a substituted heteroaryl selected from the group consisting of substituted thiazolyl, substituted thienyl, and substituted furanyl.

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- 1 7. A method in accordance with claim 5, wherein said Ar² is a
2 substituted or unsubstituted phenyl or a substituted or unsubstituted naphthyl.
- 1 8. A method in accordance with claim 3, wherein Ar² is a phenyl
2 group having from 1 to 4 substituents independently selected from the group consisting of
3 halogen, hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, (C₁-C₄)haloalkyl, (C₁-
4 C₄)haloalkoxy, nitro, cyano, (C₁-C₄)acyl, amino, (C₁-C₄)alkylamino, and di(C₁-
5 C₄)alkylamino.
- 1 9. A method in accordance with claim 8, wherein said phenyl group
2 has from 1 to 3 substituents independently selected from the group consisting of halogen,
3 (C₁-C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, and (C₁-C₄)acyl.
- 1 10. A method in accordance with claim 3, wherein Ar¹ is a substituted
2 or unsubstituted monocyclic or bicyclic heterocycle.
- 1 11. A method in accordance with claim 10, wherein said heterocycle is
2 selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl,
3 isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxadiazolyl,
4 purinyl, benzimidazolyl, indolyl, isquinolyl, quinoxalinyl and quinolyl.
- 1 12. A method in accordance with claim 11, wherein said heterocycle is
2 selected from the group consisting of thienyl, thiazolyl and benzoxadiazolyl.
- 1 13. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is selected from the group consisting of contact
3 hypersensitivity, atopic dermatitis, allergic airway hypersensitivity, allergic rhinitis,
4 atherosclerosis, septic shock, angina, myocardial infarction, restenosis,
5 ischemia/reperfusion injury, multiple sclerosis, rheumatoid arthritis, type I diabetes,
6 psoriasis, cancer and HIV infection.
- 1 14. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is psoriasis, contact hypersensitivity or atopic dermatitis.
- 1 15. A method in accordance with claim 14, wherein said CCR4-
2 mediated condition or disease is psoriasis.

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1 16. A method in accordance with claim 14, wherein said CCR4-
2 mediated condition or disease is contact hypersensitivity.

1 17. A method in accordance with claim 14, wherein said CCR4-
2 mediated condition or disease is atopic dermatitis.

1 18. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is a disease of the airway.

1 19. A method in accordance with claim 18, wherein said disease of the
2 airway is selected from the group consisting of allergic asthma and allergic rhinitis.

1 20. A method in accordance with claim 18, wherein said disease of the
2 airway is allergic asthma.

1 21. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is a disease of innate immunity.

1 22. A method in accordance with claim 21, wherein said disease of
2 innate immunity is septic shock.

1 23. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is atherosclerosis.

1 24. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is a disease or condition characterized by platelet
3 aggregation or thrombosis.

1 25. A method in accordance with claim 24, wherein said CCR4-
2 mediated disease or condition is selected from the group consisting of angina, myocardial
3 infarction, restenosis, stroke and ischemia/reperfusion injury.

1 26. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is an allergic condition and said compound is used alone or
3 in combination with at least one therapeutic agent wherein said therapeutic agent is an
4 antihistamine.

1 27. A method in accordance with claim 1, wherein said CCR4-
2 mediated disease or condition is psoriasis and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a corticosteroid, a lubricant,
4 a keratolytic agent, a vitamin D₃ derivative, PUVA, or anthralin.

1 28. A method in accordance with claim 1, wherein said CCR4-
2 mediated disease or condition is atopic dermatitis and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a lubricant and
4 corticosteroid.

1 29. A method in accordance with claim 1, wherein said CCR4-
2 mediated condition or disease is asthma and said compound is used alone or in
3 combination with at least one therapeutic agent selected from a β 2-agonist and a
4 corticosteroid.

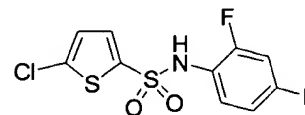
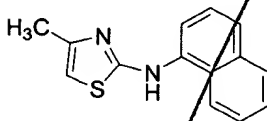
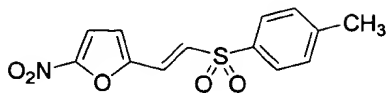
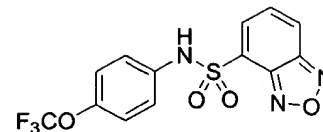
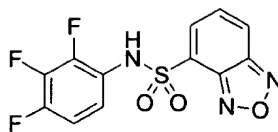
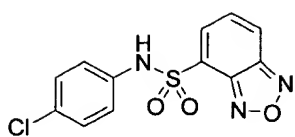
1 30. A method in accordance with claim 1, wherein said compound
2 interferes with the interaction between CCR4 and a ligand.

1 31. A method in accordance with claim 1, wherein said administration
2 is oral or intravenous.

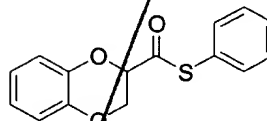
1 32. A method in accordance with claim 1, wherein said subject is
2 selected from the group consisting of human, rat, dog, cow, horse, and mouse.

1 33. A method in accordance with claim 1, wherein said subject is
2 human.

1 34. A method in accordance with claim 1, wherein said compound is
2 selected from the group consisting of



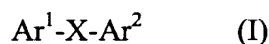
and



35. A method in accordance with claim 1, wherein said CCR4-mediated disease or condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, type I diabetes, psoriasis, cancer and HIV infection; Ar¹ is a substituted heterocycle; X is -SO₂NH-; and Ar² is a substituted phenyl.

36. A method in accordance with claim 1, wherein said CCR4-mediated disease or condition is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, type I diabetes, psoriasis, cancer and HIV infection; Ar¹ is a substituted heterocycle; X is -NH-; and Ar² is naphthyl.

37. A pharmaceutical composition for the treatment of a CCR4-mediated disease or condition, said composition comprising a pharmaceutically acceptable carrier and an effective amount of a compound which inhibits the binding of MDC or TARC to CCR4; said compound having the formula:

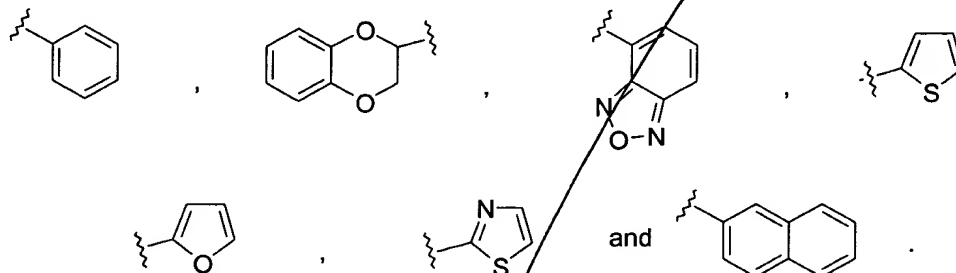


Ar¹ and Ar² are each members independently selected from the group consisting of substituted or unsubstituted aryl, substituted or unsubstituted fused aryl-heterocyclic ring systems and substituted or unsubstituted heteroaryl; and X is a linking group selected from the group consisting of -N(R)-, -C(O)S-, -CH=CHSO₂- and -SO₂N(R)- wherein R is a member selected from the group consisting of H and substituted or unsubstituted (C₁-C₈)alkyl.

38. A composition of claim 37, wherein X is -NH-.

39. A composition of claim 37, wherein X is -SO₂NH-.

1 40. A composition of claim 37, wherein Ar¹ and Ar² are each
2 substituted or unsubstituted members independently selected from the group consisting
3 of:



1 41. A composition of claim 37, wherein Ar¹ is substituted heteroaryl
2 and Ar² is substituted or unsubstituted aryl.

1 42. A composition of claim 41, wherein said Ar¹ is a substituted
2 heteroaryl selected from the group consisting of substituted thiazolyl, substituted thienyl,
3 and substituted furanyl.

1 43. A composition of claim 41, wherein said Ar² is a substituted or
2 unsubstituted phenyl or a substituted or unsubstituted naphthyl.

1 44. A composition of claim 41, wherein Ar² is a phenyl group having
2 from 1 to 4 substituents independently selected from the group consisting of halogen,
3 hydroxy, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₁-C₄)alkylthio, (C₁-C₄)haloalkyl, (C₁-
4 C₄)haloalkoxy, nitro, cyano, (C₁-C₄)acyl, amino, (C₁-C₄)alkylamino, and di(C₁-
5 C₄)alkylamino.

1 45. A composition of claim 44, wherein said phenyl group has from 1
2 to 3 substituents independently selected from the group consisting of halogen, (C₁-
3 C₄)haloalkyl, (C₁-C₄)haloalkoxy, nitro, cyano, and (C₁-C₄)acyl.

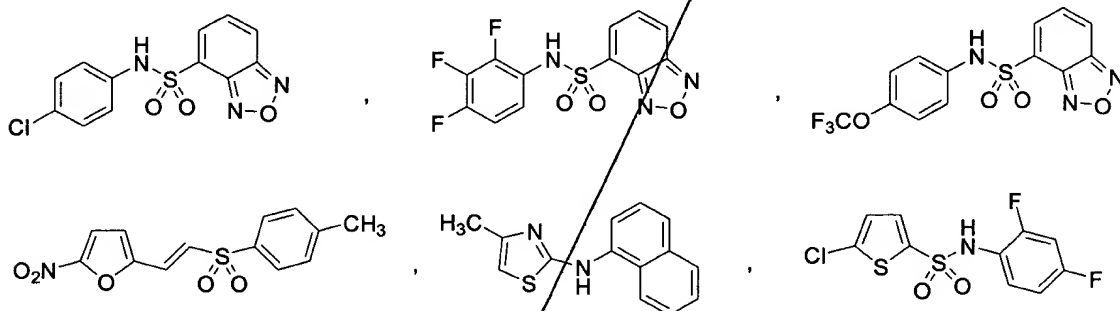
1 46. A composition of claim 37, wherein Ar¹ is a substituted or
2 unsubstituted monocyclic or bicyclic heterocycle.

1 47. A composition of claim 46, wherein said heterocycle is selected
2 from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, pyrazinyl, oxazolyl,

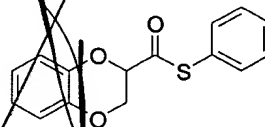
isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxadiazolyl, purinyl, benzimidazolyl, indolyl, isoquinolyl, quinoxaliny and quinolyl.

48. A composition of claim 47, wherein said heterocycle is selected from the group consisting of thienyl, thiazolyl and benzoxadiazolyl.

49. A composition of claim 37, wherein said compound is selected from the group consisting of



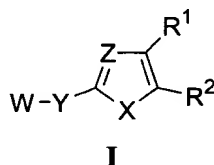
and



50. A method for modulating CCR4 function in a cell, comprising contacting said cell with a CCR4-modulating amount of a composition of claim 37.

51. A method for modulating CCR4 function, in which said cell is contacted with a CCR4 protein with a therapeutically effective amount of the composition of claim 37.

52. A compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

9 Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein
10 the integer n is 1 or 2;
11 Z is selected from N and C(R⁸);
12 R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'',
13 (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally,
14 R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3
15 heteroatoms selected from N, O and S, wherein R' and R'' are
16 independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R''
17 are attached to nitrogen atom, they may be combined with the nitrogen
18 atom to form a 5-, 6-, or 7-membered ring;
19 R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl,
20 heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;
21 R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;
22 R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and
23 heteroaryl; and
24 R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl;
25 with the provisos that R² is other than H when W is unsubstituted phenyl, X is S,
26 Y is NH, Z is N and R¹ is (C₁-C₈)alkyl; and R¹ is other than phenyl, when W is phenyl or
27 unsubstituted naphthyl, X is S, Y is NH, and Z is N.

1 53. A compound of claim 52, wherein Z is N.

1 54. A compound of claim 52, wherein X is S.

1 55. A compound of claim 52, wherein Y is N(R⁵).

1 56. A compound of claim 52, wherein Z is N, X is S and Y is N(R⁵).

1 57. A compound of claim 52, wherein W is aryl or heteroaryl.

1 58. A compound of claim 57, wherein W is substituted or unsubstituted
2 phenyl or naphthyl.

1 59. A compound of claim 57, wherein W is substituted or unsubstituted
2 pyridyl or quinolyl.

1 **60.** A compound of claim **52**, wherein R^1 and R^2 are each
2 independently selected from H and (C_1-C_8) alkyl.

1 **61.** A compound of claim **52**, wherein R^1 and R^2 are combined to form
2 a fused 6-membered aryl or heteroaryl ring.

1 **62.** A compound of claim **52**, wherein Z is N, X is S, Y is $N(R^5)$ and
2 R^1 and R^2 are each independently selected from H and (C_1-C_8) alkyl.

1 **63.** A compound of claim **52**, wherein Z is N, X is S, Y is $N(R^5)$ and
2 R^1 and R^2 are combined to form a fused 6-membered aryl or heteroaryl ring.

1 **64.** A compound of claim **52**, said compound being selected from the
2 group consisting of:

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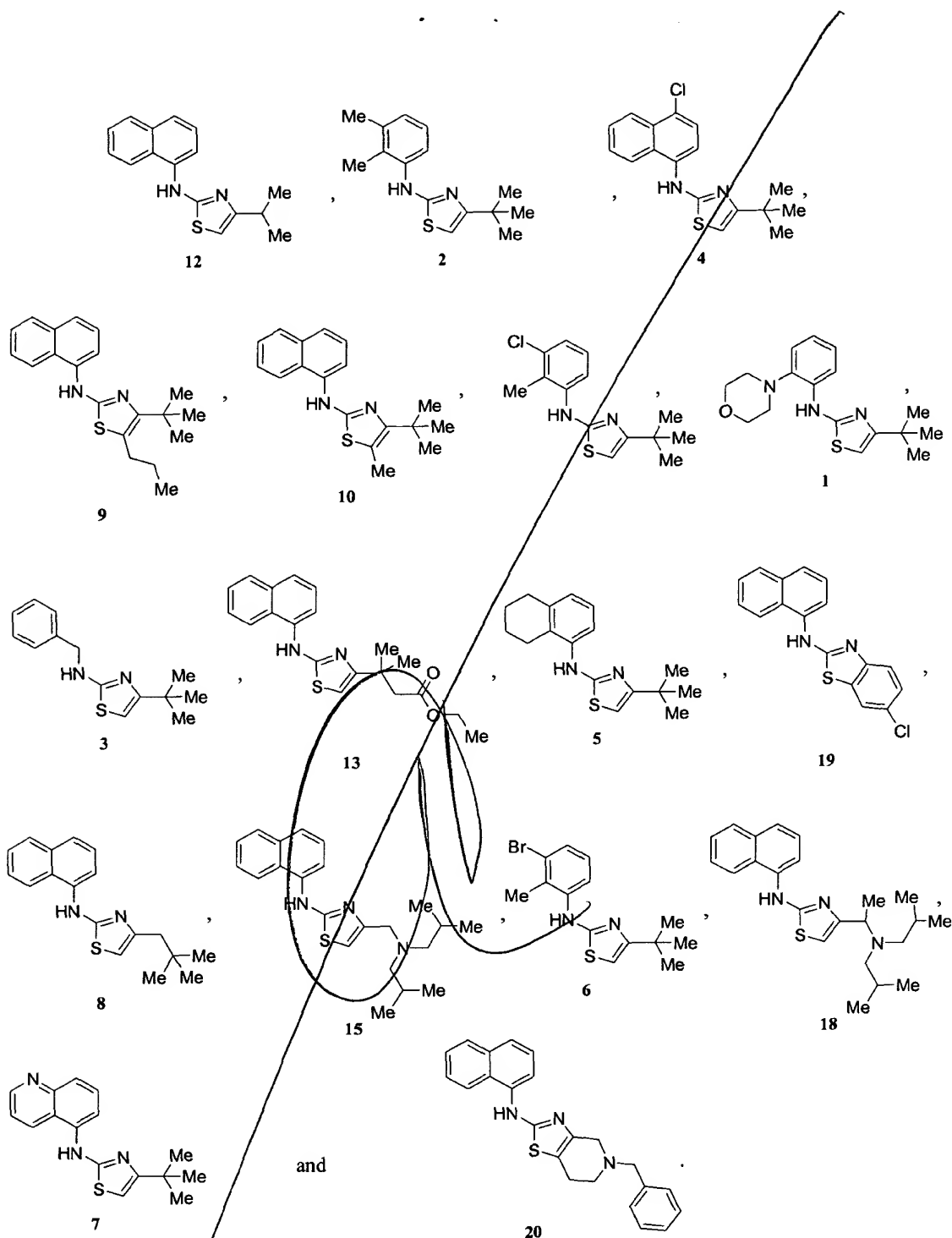
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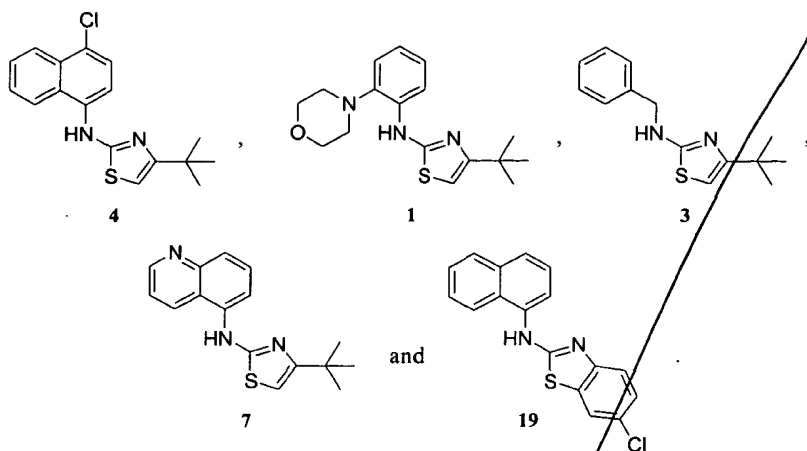
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65. A compound of claim 52, said compound being selected from the group consisting of:

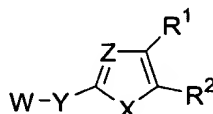




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66. A compound of claim 52, wherein
- W is selected from substituted phenyl, substituted or unsubstituted naphthyl, pyridyl, quinolyl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;
- X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);
- Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;
- Z is selected from N and C(R⁸);
- R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'', (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to a nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;
- R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;
- R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;
- R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and
- R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

- 1
67. A compound of claim 66, wherein Z is N.

- 1 68. A compound of claim 66, wherein X is S.
- 1 69. A compound of claim 66, wherein Y is N(R⁵).
- 1 70. A compound of claim 66, wherein Z is N, X is S and Y is N(R⁵).
- 1 71. A compound of claim 66, wherein W is substituted phenyl or
2 substituted or unsubstituted naphthyl.
- 1 72. A compound of claim 66, wherein W is substituted or unsubstituted
2 pyridyl or substituted or unsubstituted quinolyl.
- 1 73. A compound of claim 66, wherein R¹ and R² are independently
2 selected from the group consisting of H and (C₁-C₈)alkyl.
- 1 74. A compound of claim 66, wherein R¹ and R² are combined to form
2 a fused 6-membered aryl or heteroaryl ring.
- 1 75. A compound of claim 66, wherein W is substituted phenyl or
2 substituted or unsubstituted naphthyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are
3 independently selected from the group consisting of H and (C₁-C₈)alkyl.
- 1 76. A compound of claim 66, wherein W is substituted phenyl or
2 substituted or unsubstituted naphthyl, Z is N, X is S, Y is N(R⁵), and R¹ and R² are
3 combined to form a fused 6-membered aryl or heteroaryl ring.
- 1 77. A compound of claim 66, wherein W is substituted or unsubstituted
2 pyridyl or substituted or unsubstituted quinolyl, Z is N, X is S, Y is N(R⁵), and R¹ and R²
3 are independently selected from the group consisting of H and (C₁-C₈)alkyl.
- 1 78. A compound of claim 66, wherein W is substituted or unsubstituted
2 pyridyl or substituted or unsubstituted quinolyl, Z is N, X is S, Y is N(R⁵), and R¹ and R²
3 are combined to form a fused 6-membered aryl or heteroaryl ring.
- 1 79. A pharmaceutical composition comprising a pharmaceutically
2 acceptable carrier and a compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

Y is selected from a bond, N(R⁵), N(R⁵)-(C₁-C₈)alkylene, O, S and S(O)_n, wherein the integer n is 1 or 2;

Z is selected from N and C(R⁸);

R¹ and R² are independently selected from H, halogen, CN, CO₂R', CONR'R'', (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, N(R⁶)(R⁷), OR⁹ and optionally, R¹ and R² combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C₁-C₈)alkyl and aryl, and when R' and R'' are attached to nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

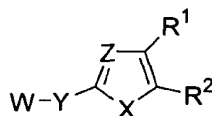
R³, R⁴ and R⁸ are independently selected from H, halogen, CN, OH, (C₁-C₈)alkyl, heteroalkyl, aryl, heteroaryl, O(C₁-C₈)alkyl, N(R⁶)(R⁷) and OR⁹;

R⁵ is selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl;

R⁶ and R⁷ are independently selected from H, (C₁-C₈)alkyl, heteroalkyl, aryl and heteroaryl; and

R⁹ is selected from (C₁-C₈)alkyl, heteroalkyl and haloalkyl.

80. A method for treating a CCR4-mediated condition in a subject, said method comprising administering to a subject in need of such treatment an effective amount of a compound of of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein

W is selected from aryl, heteroaryl, (C₁-C₈)alkyl, heteroalkyl, cycloalkyl and heterocycloalkyl;

X is selected from N(R⁵), S, O, C(R³)=C(R⁴), N=C(R⁴) and, optionally, when Z is N, X can be C(R⁶)(R⁷);

Y is selected from a bond, $N(R^5)$, $N(R^5)-(C_1-C_8)$ alkylene, O, S and $S(O)_n$, wherein the integer n is 1 or 2;

Z is selected from N and $C(R^8)$;

R^1 and R^2 are independently selected from H, halogen, CN, CO_2R' , $CONR'R''$, (C_1-C_8) alkyl, heteroalkyl, aryl, heteroaryl, $N(R^6)(R^7)$, OR^9 and optionally, R^1 and R^2 combine to form a 5- to 8-membered ring containing from 0 to 3 heteroatoms selected from N, O and S, wherein R' and R'' are independently selected from H, (C_1-C_8) alkyl and aryl, and when R' and R'' are attached to nitrogen atom, they may be combined with the nitrogen atom to form a 5-, 6-, or 7-membered ring;

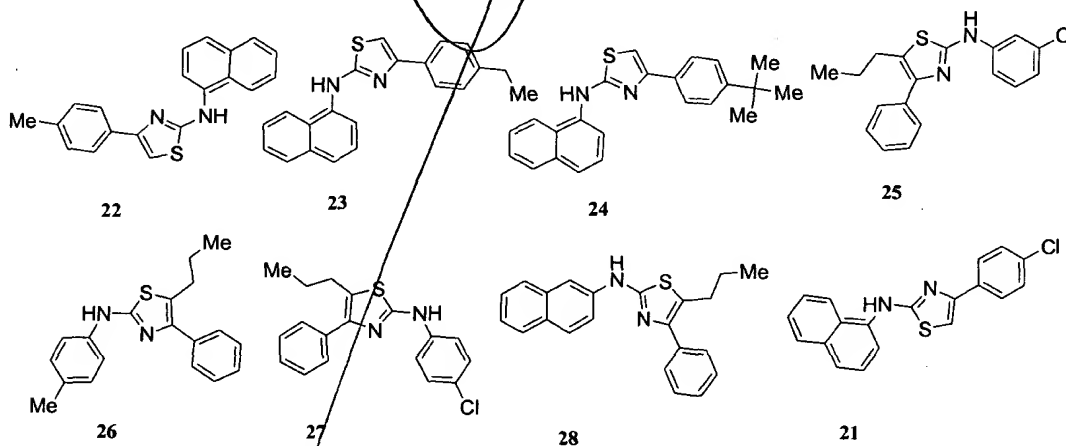
R^3 , R^4 and R^8 are independently selected from H, halogen, CN, OH, (C_1-C_8) alkyl, heteroalkyl, aryl, heteroaryl, $O(C_1-C_8)$ alkyl, $N(R^6)(R^7)$ and OR^9 ;

R^5 is selected from H, (C_1-C_8) alkyl, heteroalkyl, aryl and heteroaryl;

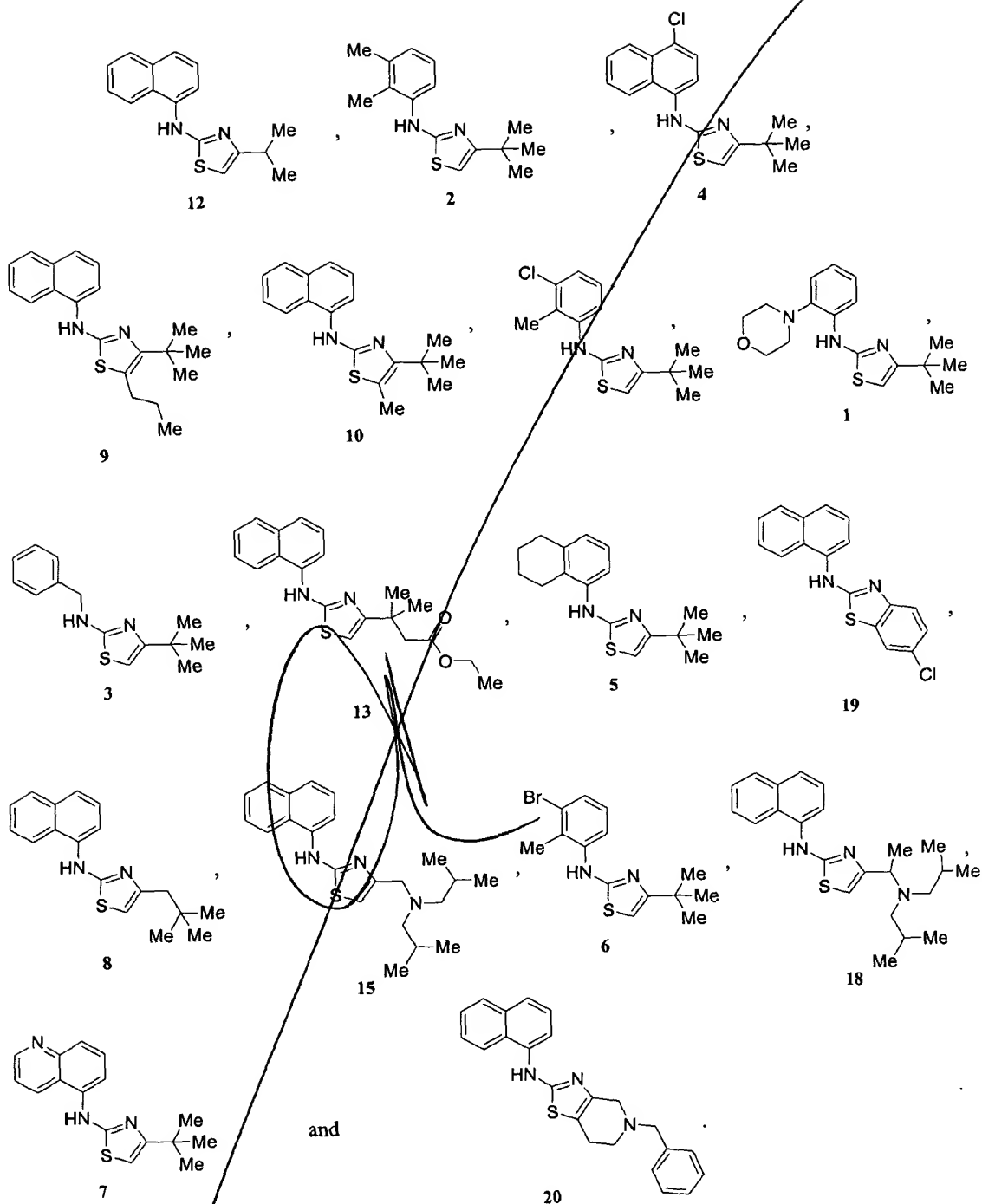
R^6 and R^7 are independently selected from H, (C_1-C_8) alkyl, heteroalkyl, aryl and heteroaryl; and

R^9 is selected from (C_1-C_8) alkyl, heteroalkyl and haloalkyl.

81. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound selected from the group consisting of:

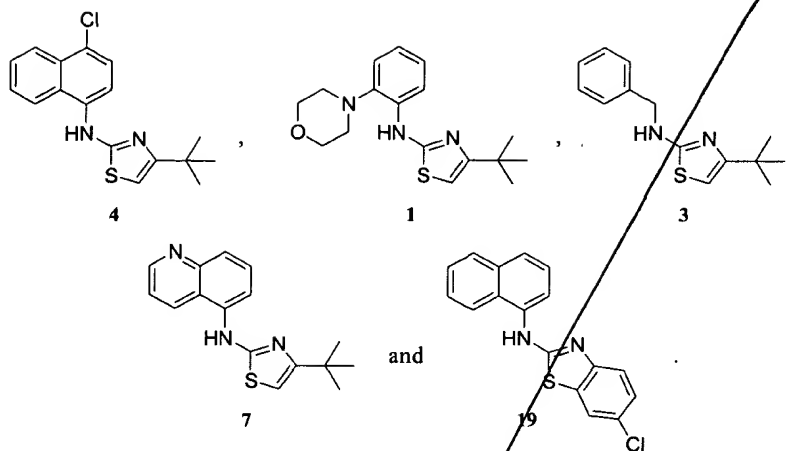


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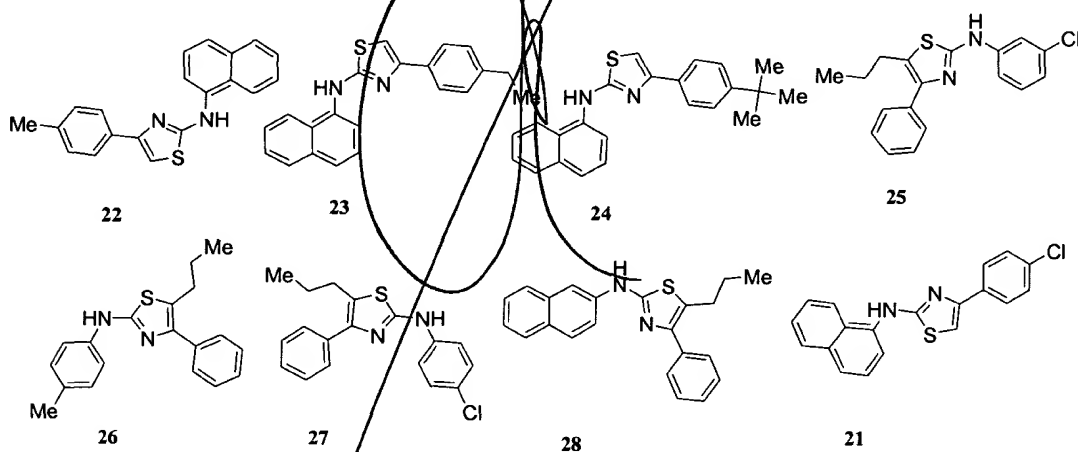


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1 **82.** A pharmaceutical composition of claim **81**, wherein said
2 compound is selected from the group consisting of:



83. A method for treating a CCR4-mediated condition in a subject, said method comprising administering to a subject in need of such treatment an effective amount of a compound selected from the group consisting of:

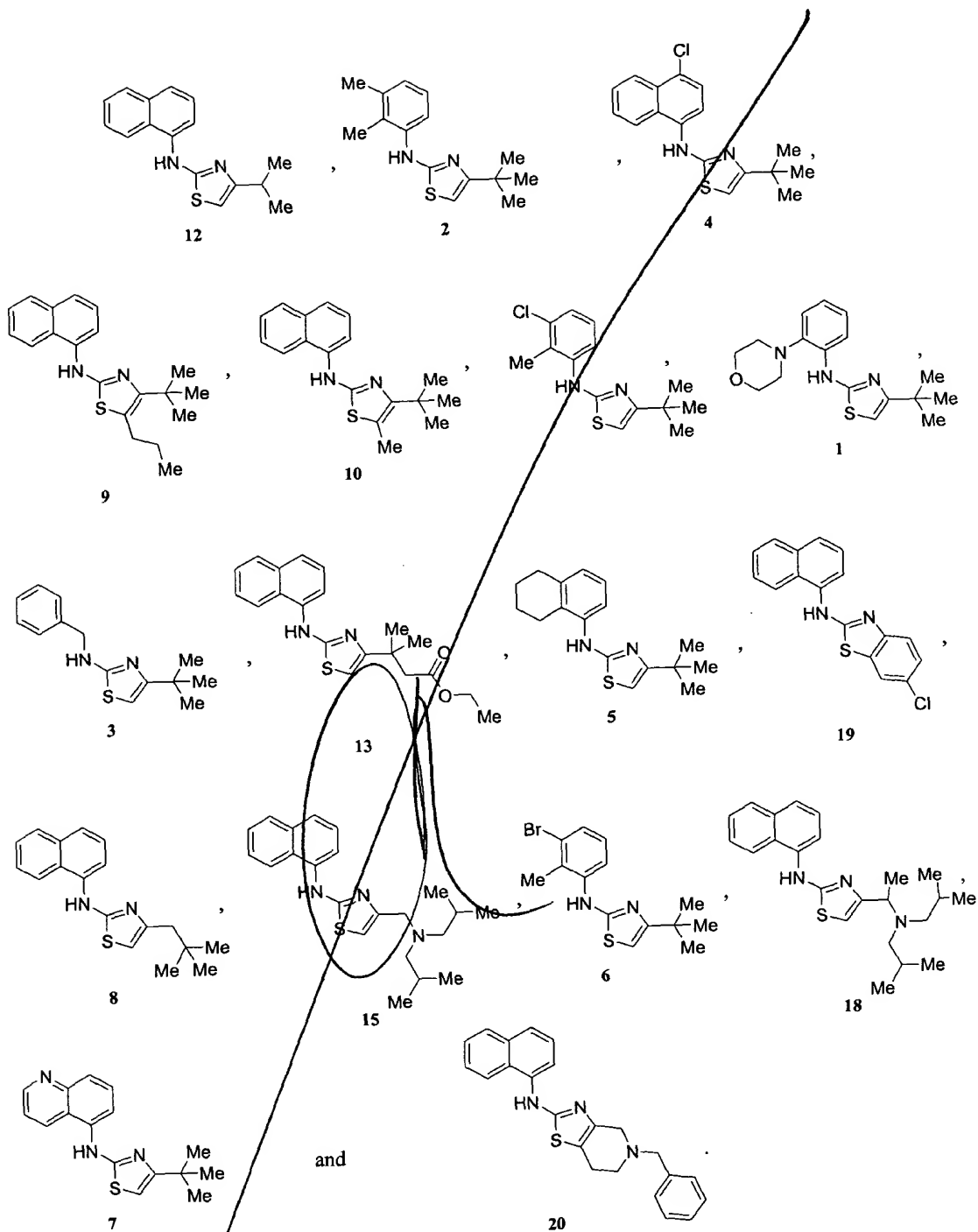


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~~84.~~ A method in accordance with claim 83, wherein said compound is the group consisting of:



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